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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/000,213	11/14/2001	Brenda F. Baker	RTS-0327	1275

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EXAMINER	
GIBBS, TERRA C	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 07/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/000,213	BAKER ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9,11-15 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-9,11-15 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission mailed on May 14, 2004 has been entered.

Claims 3, 10, and 16-29 have been canceled. Claims 1 and 11-15 have been amended. New claim 30 is acknowledged.

Claims 1, 2, 4-9, 11-15, and 30 have been examined on the merits.

Response to Arguments

Applicants Amendment and Response mailed May 14, 2004 has been considered. Rejections and/or objections not reiterated from the previous office action mailed November 19, 2003 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Change in Power of Attorney

Applicants Change in Power of Attorney under 37 CFR §3.73(b) is acknowledged.

Claim Objections

Claim 30 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. For example, claim 1 is drawn to an oligonucleotide which specifically hybridizes within nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) and inhibits the expression of human vitamin D nuclear receptor. Claim 30 is drawn to oligonucleotides of claim 1 comprising SEQ ID NOs: 53-56. It is noted that SEQ ID NOs. 53-56 overlap exactly with nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) as recited in claim 1. Since claim 30 does not further limit the subject matter of claim 1, Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-9, 11-15, and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Cowsert et al. [U.S. Patent No. 6,566,131].

Claim 1 is drawn to an oligonucleotide which specifically hybridizes within nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) and inhibits the expression of human vitamin D nuclear receptor. Claims 2, 4-9, and 11-14 are dependent on claim 1 and include all the limitations of claim 1, with the further limitations wherein the oligonucletoide is an antisense; wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage; wherein the modified internucleoside linkage is a phosphorothioate linkage; wherein the antisense oligonucleotide comprises at least one modified sugar moiety; wherein the sugar moiety is a 2'-O-methoxyethyl sugar moiety; wherein the antisense oligonucleotide comprises at least one modified nucleobase; wherein the modified nucleobase is a 5-methylcytosine; wherein the antisense oligonucleotide is a chimeric oligonucleotide; and a composition comprising an oligonucleotide which specifically hybridizes within nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) and a pharmaceutically acceptable carrier or diluent, further comprising a colloidal dispersion system. Claim 15 is drawn to a method of inhibiting the expression of vitamin D nuclear receptor in cells or tissues comprising contacting said cells or tissues in vitro with an oligonucleotide which specifically hybridizes within nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) so that expression of vitamin D nuclear receptor is inhibited. Claim 30 is dependent on claim 1 and includes all the limitations of claim 1 with the further limitation, wherein said compound comprises a sequence of SEQ ID NOs: 53-56.

Cowsert et al. disclose a modified antisense oligonucleotide targeted to Smad6 with the following sequence: 5'- gggtccgttccctcaac-3' (see SEQ ID NO:23). Cowsert et al. further

disclose that the antisense oligonucleotide targeted to Smad6 was effective *in vitro* (see Table 1). This antisense oligonucleotide is reverse complementary to bases 1723-1738 of SEQ ID NO:3 of the instant invention. It is noted that the reverse complimentarity between the antisense oligonucleotide targeted to Smad6 disclosed by Cowsert et al. and nucleobases 1723-1738 of SEQ ID NO:3 is not contiguous. However, the antisense oligonucleotide targeted to Smad6 disclosed by Cowsert et al. exhibits almost 94% local similarity to nucleobases 1723-1738 of SEQ ID NO:3 of the instant invention, as it contains only one mismatch (see attached sequence alignment). Given this high degree of similarity, the antisense oligonucleotide targeted to Smad6 disclosed by Cowsert et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" since the instant specification at page 10, lines 9-12 teaches, "it is understood in the art that the sequence of an antisense compound need not be 100% complementary to that of its target nucleic acid to be specifically hybridizable." Accordingly, the antisense oligonucleotide disclosed by Cowsert et al. would specifically hybridize to bases 1723-1738 of SEQ ID NO:3 as claimed. Regarding claim 30, which recites specific antisense sequences, it is noted that SEQ ID NOs. 53-56 (as recited in claim 30) overlap exactly with nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) as recited in claim 1. Therefore, the antisense oligonucleotide disclosed by Cowsert et al. reads on this claim as well. Further, the burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression of human vitamin D nuclear receptor as instant claimed falls to Applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical

processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2122 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the antisense oligonucleotide disclosed by Cowsert et al. would or would not have the additional "functional limitation" of "inhibiting expression" of human vitamin D nuclear receptor.

Therefore, absent evidence to the contrary, claims 1, 2, 4-9, 11-15, and 30 are anticipated by Cowsert et al.

Claims 1, 2, 4, 5, 6, 8, 9, 12, 13, 14, and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Gimeno et al. [U.S. Patent No. 5,955,306].

Claims 1, 2, 4, 5, 6, 8, 9, 12, 13, and 14 are drawn to the invention as described above in the 35 U.S.C. 102(e) rejection against claims 1, 2, 4-9, 11-15, and 30 as being anticipated by Cowsert et al. [U.S. Patent No. 6,566,131].

Gimeno et al. disclose a modified antisense oligonucleotide targeted to Tub Interactor with the following sequence: 5'-ccctcagcgtcagtcagc-3' (see SEQ ID NO:27). This antisense

oligonucleotide is reverse complementary to bases 1714-1731 of SEQ ID NO:3 of the instant invention. It is noted that the reverse complimentarity between the antisense oligonucleotide targeted to Tub Interactor disclosed by Gimeno et al. and nucleobases 1714-1731 of SEQ ID NO:3 is not contiguous. However, the antisense oligonucleotide targeted to Tub Interactor disclosed by Gimeno et al. exhibits almost 89% local similarity to nucleobases 1714-1731 of SEQ ID NO:3 of the instant invention, as it contains only two mismatches (see attached sequence alignment). Given this high degree of similarity, the antisense oligonucleotide targeted to Tub Interactor disclosed by Gimeno et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" since the instant specification at page 10, lines 9-12 teaches, "it is understood in the art that the sequence of an antisense compound need not be 100% complementary to that of its target nucleic acid to be specifically hybridizable." Accordingly, the antisense oligonucleotide disclosed by Gimeno et al. would specifically hybridize to bases 1714-1731 of SEQ ID NO:3 as claimed. Regarding claim 30, which recites specific antisense sequences, it is noted that SEQ ID NOs. 53-56 (as recited in claim 30) overlap exactly with nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) as recited in claim 1. Therefore, the antisense oligonucleotide disclosed by Gimeno et al. reads on this claim as well. Further, the burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression of human vitamin D nuclear receptor as instant claimed falls to Applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not

necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2122 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the antisense oligonucleotide disclosed by Gimeno et al. would or would not have the additional "functional limitation" of "inhibiting expression" of human vitamin D nuclear receptor.

Therefore, absent evidence to the contrary, claims 1, 2, 4, 5, 6, 8, 9, 12, 13, and 14 are anticipated by Gimeno et al.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (571) 272-0758. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
July 12, 2004

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